REMARKS

Claims 26-44 and 47-62 are pending in the present application with claims 49-62 having been added by way of this amendment.

Claims 26, 28, 29, 31, 33, 34 and 35 stand rejected under 35 U.S.C. 112, second paragraph. Applicants respectfully traverse this rejection for the following reasons. In each of the pending claims 26, 28, 29, 31, 33, 34 and 35, an apparatus is recited and the function of the calibration device is positively recited in the claim in that the calibration device at least partly compensates fro an alteration of the value of the physical parameter of the sensor element, the physical parameter being the threshold voltage of the measuring transistor. Applicants therefore believe that all of the above claims comply with 25 U.S.C. 112, second paragraph, and kindly request that the Examiner withdraw this rejection since it is clear as to what type of calibration device is being recited in the claim since the manner in which it functions is clearly positively set forth.

Claim 35 stands rejected under 35 U.S.C. 112, second paragraph. Applicants respectfully traverse this rejection for the following reasons. Applicants respectfully note to the Examiner that claim 35 positively recites a calibration device which is set up such that it is used to convert a sensor signal of the sensor element. The sensor signal is brought about by a sensor event using the principle of correlated double sampling to a value is independent of the value of the physical parameter of the sensor element. The "principle of correlated double sampling" is described in detail in the present specification (page 57, line 25 to page 50, line 11). Accordingly, Applicants respectfully submit that this term is sufficiently described and supported by the specification. Furthermore, Applicants believe that the "principle of correlated double sampling" is a method well known to one of skill in the art. As a result of the foregoing, Applicants believe that claim 35 is sufficiently clear and does recite a step of setting up or configuring the calibration device in a certain manner. Reconsideration and withdrawal of this rejection are earnestly solicited.

In response to the Examiner's rejection of claims 30 and 32 under 35 U.S.C. 112, second paragraph, Applicants have amended each of these claims. Withdrawal of the rejection is now in order.

Claims 40, 44, 45 and 46 stand rejected due to the presence of the expression "and/or". Applicants have amended claims 40 and 44 to eliminate this expression and claims 45 and 46 have been canceled. Withdrawal of this rejection is in order in view of the present amendments. In addition, as a result of these changes, Applicants have added a set of new claims to capture all of the subject matter presented in original claims 40, 44, 45 and 46.

Claims 26-33, 35, 37, 39, 41 and 42 stand rejected under 35 U.S.C. 102(b) as being anticipated by U.S. patent No. 5,309,085 to Sohn. Claims 34, 36, 40 and 43-48 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Sohn and further in view of Thewes (WO 01/75462). Applicants respectfully traverse these rejections for the following reasons.

Before discussing the above rejections in detail, Applicants believe that a brief discussion of the present invention is in order and will assist the Examiner in appreciating the differences between the present invention and the disclosures of the prior art references.

The present invention is based on the problem of providing an electronic multi-electrode array in which, even in the event of an alteration or a deviation of the value of a physical parameter of a sensor element from a reference value, i.e. a value of the physical parameter that occurs under normal, preferably predetermined, process conditions, a sensor signal generated by the sensor element is independent of the alteration of the value. This problem is resolved by means of the circuit arrangement, the sensor array and the biosensor array as specified in the present patent application. A key element of the present invention is that it can be used to at least partly compensate for an alteration of the value of the physical parameter of the sensor element, said physical parameter being the threshold voltage of a measuring transistor.

The prior art document of Sohn (U.S. Patent No. 5,309,085; henceforth Sohn) teaches a measuring circuit using a biosensor which comprises two ion sensitive field effect transistor

(ISFET) input devices and a differential amplifier 50 for ampliflying the outputs of the two ISFETs. A first ISFET, referred to as ENFET 10, comprises an ion sensitive membrane 4 which is formed on the gate and the circumference of a metal contact 3 (which acts as a source or drain terminal of the ISFET), and an enzyme sensitive membrane 1 which is formed over the ion sensitive membrane. The second ISFET, referred to as reference FET or REFET 20, differs from the ENFET in having no enzyme sensitive membrane. When the biosensor is soaked in a solution of a specific biomaterial or substrate S, the enzyme sensitive membrane 1 of the ENFET 10 reacts upon the specific biomaterial in the solution resulting in a signal from the ENFET 10 which depends on the concentration of the biomaterial in the solution. On the other hand, since the REFET 20 has no enzyme sensitive membrane, the signal detected from the REFET 20 is independent of the substrate concentration. In addition, a quasi-reference electrode (QRE), made of Pt or Au, acts as a reference electrode having a non-stable performance in the solution. The output voltage of the ENFET with enzyme sensitive membrane is a function of the substrate concentration pS and the non-stable potential Vq of the solution due to the use of QRE. On the other hand, the output voltage of the REFET which is not responsive to pS is a function of Vq only. A final voltage, which is a function of pS only, is obtained by applying the output voltages of the ENFET and the REFET to a differential amplifying circuit.

In the outstanding Office Action, the Examiner equates the claimed sensor element of the present patent application to the element 30 in the Sohn reference (shown in Fig. 3) and states that this sensor element has an electrode 3 that is coupled to a substance to be examined. However, the element 30, which is not specifically identified in the specification of Sohn, is merely the quasi-reference electrode QRE which is connected to a power supply and is placed in the solution. Thus, element 30 clearly cannot be identified with the claimed sensor element having an electrically conductive sensor electrode and a measuring transistor (see e.g., pending claim 26 of the present patent application). Furthermore, reference numeral 3 in the Sohn reference denotes the metal contacts on the source/drain regions of the ISFET (see Fig. 1) which are not coupled to a substance to be measured, but rather are electrically insulated by an electrical insulating material 2 (see Fig. 1). Thus, it is unclear as to what the Examiner is referring to as the sensing element. The Examiner

further equates the reference FET (REFET) 20 to the calibration device of the present patent application. As mentioned above, the REFET 20 lacks the enzyme sensitive membrane 1 and is therefore not responsive to the specific substrate. The REFET 20 merely serves as an input device of the differential amplifier 50. From the specification of the present patent application it becomes clear that the claimed calibration device differs significantly from the REFET 20 of the Sohn reference. The calibration device, as recited in pending claim 26, is set up such that it at least partly compensates for an alteration of the value of the physical parameter of the sensor element, the physical parameter being the threshold voltage of the measuring transistor.

The Sohn reference does not teach that the REFET 20 performs this function.

As explained in the specification of the present patent application, the compensation is achieved by setting up the calibration device in such a way that it can be used to control the electrical potential present at a second source/drain terminal of the measuring transistor with the calibration realized by means of a source negative feedback of the calibration transistor with respect to the measuring transistor. In an alternative embodiment of the present invention the compensation is achieved by setting up the calibration device in such a way that it can be used to control the electrical potential present at a first source/drain terminal of the measuring transistor with the calibration transistor being operated as a gate-controlled source follower in this case. Thus, the specific arrangement and connection between the calibration device, i.e., the calibration transistor, and the measuring transistor as taught by the present patent application, is not disclosed in the Sohn reference. In addition, the manner in which the calibration device acts is likewise not disclosed in the Sohn reference. The REFET of the Sohn reference is not concerned with calibration of the current through a first source/drain terminal of the measuring transistor by action of the calibration device, either by means of a source negative feedback as in Fig. 2 of the present application. Other components of the claimed biosensor circuit, including the switching devices (Fig. 2) or potential control device (Fig. 3) are likewise absent in the Sohn reference.

The prior art document of Krauss et al. (U.S. Patent No. 5,602,467; henceforth Krauss) teaches a circuit layout for measuring ion concentrations in solutions using ion-sensitive field effect

transistors (ISFET) with a reference electrode 16 made from electrically good conducting, chemically resistant, materials such as gold or platinum. However, the Krauss reference does neither disclose nor teach a biosensor circuit as claimed in the present patent application.

The prior art document of Thewes (WO 01/75462 A1; henceforth Thewes) teaches a sensor array with transistors which are configured as sensors. The sensors of the sensor array are arranged in rows and columns. However, the specific arrangement and connection between the individual transistors in the sensor array disclosed in the Thewes reference are substantially different from the biosensor circuit arrangement as described in the present patent application.

One aspect of the present invention lies in the reduction of the required electrical current of the biosensor. This is achieved by the sensor array as specified in the present patent application. The circuit arrangement of the sensor according to the invention has the feature that the components of the circuit arrangement, in particular the sensor elements and the calibration device, can be integrated into a substrate. This brings about a miniaturization of the arrangement, which in turn not only improves the spatial resolution of the sensor array but also leads to a reduction of the required electrical current. Another important aspect of the present invention is that, by at least partly compensating for an alteration of the value of the physical parameter of the sensor element (e.g. the threshold voltage of the measuring transistor), using the calibration device (e.g. calibration transistor) an unambiguous assignment of a sensor element to a sensor event becomes possible even if the respective physical parameter, e.g. the threshold voltage of the measurement transistor, varies from around a mean value between different sensor elements, for example on account of process fluctuations. Thus, by compensating for an alteration of the threshold voltage measurement transistor the reproducibility and the measurement accuracy of the sensor element or measuring transistor are significantly improved. In addition, as fluctuations of the threshold voltages between different measuring transistors around a mean value are compensated for by the calibration device, an overly high exactness in the production of the sensor element of the sensor array is dispensable. A miniaturization of transistor-based sensors is disclosed in the Thewes reference, the circuit arrangement though being substantially different from the one disclosed in the present patent application. However, none of the cited prior art documents teaches or even suggests how to

combine a sensor element as specified in the present application, comprising an electrically conducting sensor electrode and a measuring transistor, with a calibration device, said calibration device being set up such that an alteration of a physical parameter (threshold voltage of the measuring transistor) can at least partly be compensated for, or how to arrange a plurality of such sensor elements into an array. As mentioned above, neither does the biosensor disclosed in the Sohn reference proved for a calibration device (the REFET 20 does not perform this function) nor does the specification indicate that there is a sensor electrode formed in or on the substrate (element 30 Sohn reference merely represents a reference electrode). Applicant therefore believes that the subject matter disclosed in the presently pending patent claims 26-44 and 47-62 is novel and inventive and is not rendered obvious by the prior art references, either taken alone or in combination..

In conclusion, nothing in the cited prior art gives any hint to a person skilled in the art leading to the technical teaching as presently claimed. Therefore, Applicants respectfully and earnestly submit that pending claims 26-44 and 47-62 meet the requirements of patentability.

Applicant respectfully requests the Examiner withdraw the rejection of the claims under U.S.C. 102 and 103.

In view of the above amendment, applicant believes the pending application is in condition for allowance.

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Respectfully submitted,

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